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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,866	04/14/2004	Lawrence J. Stern	07917-212001 / UMMC 03-10	6194
26161 7590 04/09/2007 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER JUNG, UNSU	
			ART UNIT	PAPER NUMBER
			1641	

  

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/823,866

Applicant(s)

STERN ET AL.

Examiner

Unsu Jung

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 January 2007.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-52 is/are pending in the application.  
4a) Of the above claim(s) 10, 14, 18 and 24-52 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-9, 11-13, 15-17, 19-23, and 25 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.  
10) ☒ The drawing(s) filed on 14 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 7/14/04 & 3/20/06  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group I (claims 1-25) in the reply filed on January 29, 2007 is acknowledged. Further, Applicant's election of species streptavidin from List I and IFN- $\gamma$  from List IV is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

With respect to the species election of biotin-streptavidin for List II(a) and II(b), anti-CD11a for List III(a), and B7-1 for List III(b), election of species for Lists II(a), II(b), III(a), and III(b) is not proper as Lists II and III each contain species (indicated by letters) and subspecies (indicated by lower case Roman numerals). During a telephone conversation with Ms. DeYoung on March 29, 2007 a provisional election was made without traverse to prosecute the species a(iii) immobilization via MHC molecule via biotin-streptavidin interaction from List II and species a(ii) anti-CD11a from List III, claims 12 and 13. Affirmation of this election must be made by applicant in replying to this Office action. Claims 10, 14, 18, and 24-52 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

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2. Claims 1-52 are pending, claims 10, 14, 18, and 24-52 are withdrawn, and claims 1-13 and 15-25 are under consideration for their merits.

### ***Information Disclosure Statement***

3. The information disclosure statements (IDS) submitted on July 14, 2004 and March 20, 2006 have been considered by the examiner. However, the following corrections have been made on IDS submitted on July 14, 2004:

- C17 (Gorga et al.): publication year has been corrected to 1987;
- C24 (Janeway et al.): place of publication and relevant page numbers have been included; and
- C58 (Wang et al.): end page number has been included.

### ***Oath/Declaration***

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

It is not clear whether the alterations made for Gregory J. Carven occurred on the same date as the signature date.

### ***Specification***

5. The use of the trademark CY<sup>®</sup> (p28) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### ***Claim Objections***

6. Claims 21-24 are objected to because of the following informalities: claims 21-24 currently depend from claim 18. However, this dependency seems to be a typo as the limitations of claim 18 is not consistent with dependent claims 21-24 (i.e. claim 23 include a limitation of MHC-peptide complexes immobilized on the substrate via the MHC molecules, which is inconsistent with the limitation of claim 18, which requires that the MHC-peptide complexes are immobilized via the antigen-derived peptide). Further clarification is necessary. For the purpose of examination, claims 21-24 have been interpreted as being dependent on claim 19. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In claim 8, the term "another molecule" is vague and indefinite. The specification does not define the term and it is unclear what the term "another molecule" means.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1, 11, 12, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Webb et al. (WO 97/46256, Dec. 11, 1997).

Webb et al. anticipates instant claims by teaching an array (see entire document) comprising a substrate (support, p49, lines 7-18) and an array of MHC molecules complexed with antigen-derived peptides (p18, lines 9-17 and p50, line 1-p51, line 25))

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immobilized in spatially distinct areas on the substrate (wells of microtiter plates, p80, lines 24-31).

With respect to claims 11 and 12, Webb et al. teaches an array, further comprising costimulatory molecules immobilized in the spatially-distinct areas on the substrate (p49, lines 7-14), wherein the costimulatory molecules are costimulatory antibodies (p21, line 27-p22, line 6).

With respect to claim 16, Webb et al. teaches an array, wherein the MHC molecules comprise class II MHC molecules (p18, lines 20-30).

12. Claims 1-3, 6, 7, 11, 15, and 16 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Brown et al. (U.S. PG Pub. No. US 2003/0044389 A1, Mar. 6, 2003 and Filed on July 2, 2002).

Brown et al. anticipates instant claims by teaching an array (see entire document) comprising a substrate (p1, paragraph [0008] and p2, paragraph [0024]) and an array of MHC molecules complexed with antigen-derived peptides immobilized in spatially-distinct areas on the substrate (p2, paragraphs [0025] and [0026]).

With respect to claim 2, Brown et al. teaches the MHC-molecules in all of the spatially-distinct areas are the same (p2, paragraph [0025]).

With respect to claims 3 and 15, Brown et al. teaches the array comprising at least about 10, 50 or 100 different MHC-peptide complexes (p4, paragraph [0042])

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With respect to claims 6 and 7, Brown et al. teaches the substrate comprising glass, quartz, polystyrene, polycarbonate, polypropylene, or silicon (p3, paragraph [0037]).

With respect to claim 11, Brown et al. teaches an array further comprising costimulatory molecules immobilized in spatially distinct areas on the substrate (p7, paragraph [0077]).

With respect to claim 16, Brown et al. teaches the MHC molecules comprise Class I MHC molecules, Class II MHC molecules, or Class I and Class II MHC molecules (p7, paragraph [0074]).

### ***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.



15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 2-7 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Taylor (U.S. Patent No. 6,103,479, Aug. 15, 2000).

Webb et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 11 above). However, Webb et al. fails to teach an array, wherein the MHC molecules in all the spatially distinct areas are the same and the spatially distinct areas are each surrounded by a hydrophobic barrier.

Taylor teaches arrays for simultaneous analysis of multiple types of cell interactions (see entire document, particularly, column 6, lines 40-47). The arrays of Taylor encompass arrays that comprise identical cell types that can be treated with a

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combinatorial of distinct compounds (different specific cell binding molecules) or a combinatorial cell types that can be treated with one or more compounds (the same specific cell binding molecules, column 6, lines 48-55). The micro-patterned chemical array comprises a base (substrate), which is treated to produce a hydrophobic surface across which are dispersed at regular intervals of hydrophilic spots or wells (spatially-distinct areas on the substrate, column 8, lines 34-37). The cells are bound only in the wells, because the specific chemical environment in the wells, in conjunction with the hydrophobic environment surrounding each of the wells, permits the selective binding of the cells to the wells only (column 11, lines 64-67). Modification of wells with specific cell binding molecules (immobilized specific cell binding molecules) permits selective binding of cells to specific wells (column 12, lines 1-3).

With respect to claims 5 and 15, Taylor teaches the array comprising at least about 10, 50, or 100 different spatially-distinct areas on the substrate, each having different specific cell binding molecules (column 6, lines 48-55 and column 16, lines 39-54).

With respect to claims 6 and 7, Taylor teaches that the substrate comprises glass or silicon (column 8, lines 34-40).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the substrate of Taylor, which includes each of the spatially-distinct areas surrounded by hydrophobic barrier and having either one type of compounds (the same MHC molecules) or a combinatorial of distinct compounds (different MHC molecules) in the array of Webb et al. in order to conduct simultaneous

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analysis of multiple types of cell interactions. The advantage of using substrate, which allows selective binding of the cells of interest to the spatially-distinct areas only and simultaneous analysis of multiple types of cell interactions provides the motivation to employ the substrate of Taylor in the array of Webb et al. with a reasonable expectation of success as the substrate of Taylor can be used for a variety of cell interactions including lymphocytes such as T-cells.

17. Claims 8, 9, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Tom-Moy et al. (U.S. Patent No. 6,235,488, May 22, 2001).

Webb et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 11 above). Webb et al. further teaches that biotinylated MHC molecules can be immobilized on the avidin-coated substrate via biotin-avidin linked interactions with the substrate (p81, lines 10-16). However, Webb et al. fails to teach that streptavidin can be used in place of avidin.

Tom-Moy et al. teaches that streptavidin can be a substitute for avidin since it has similar biotin-binding properties (see entire document, particularly column 4, lines 62-63).

Therefore, Webb et al. meets the limitations of claims 8 and 9 except that it employs avidin rather than streptavidin to coat the substrate surface for immobilization

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of biotinylated MHC molecules. However, because these two elements were art-recognized equivalents at the time of the invention in the specific binding applications, where it is immaterial whether the avidin or streptavidin is used to bind to a biotin, one of ordinary skill in the art at the time of the invention would have found it obvious to substitute streptavidin for the avidin of Webb et al.

18. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Abraham et al. (*J. Immunol.*, 20014, Vol. 167, pp5193-5201) and Mikesell et al. (U.S. PG Pub. No. US 2002/0095024, Filed on June 6, 2001).

Webb et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 11 above). Webb further teaches the costimulatory molecules include ICAM's (ICAM-1, ICAM-2, and ICAM-3, p72, line 14-p74, line 20). Activation of T cells is characterized by proliferation of the responsive T cell population coordinated with the selection of cytokines (p16, lines 28-32). However, Webb et al. fails to teach an array, wherein the costimulatory antibodies bind specifically to CD11a.

Abraham et al. teaches that integrin LFA-1 serves as an accessory molecule in T cell activation (see entire document). The primary pathway whereby engagement of LFA-1 through its ligand ICAM-1 up-regulates IL-2 gene expression through enhanced

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IL-2 transcription (Abstract). Further, a number of anti-LFA-1 Abs has agonist/costimulatory activity such as anti-CD11a mAb (p5197, right column).

Mikesell et al. teaches that a first signal mediated by foreign antigens presented by MHC complexes causes T-cell entry into the cell cycle and a second signal, termed costimulation, causes cytokine production and T-cell proliferation (p1, paragraph [0003]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include anti-CD11a antibody of Abraham et al. as a costimulatory antibodies in the array of Webb et al. in order to provide costimulatory signal in addition to the antigenic signal of the MHC molecules complexed with antigen-derived peptides necessary for production of cytokines and T-cell proliferation, which can be used to detect T-cell activation/responsiveness. The advantage of delivering necessary costimulatory signal for T-cell characterization provides the motivation to combine teachings of Webb et al. and Abraham et al. with a reasonable expectation of success as Mikesell et al. teaches that a first signal mediated by foreign antigens presented by MHC complexes causes T-cell entry into the cell cycle and a second signal, termed costimulation, causes cytokine production and T-cell proliferation. Further, Webb et al. meets the limitations of claim 13 except that it employs an ICAM's rather than anti-CD11a antibodies as costimulatory molecules. However, because these two elements were art-recognized equivalents at the time of the invention in the T-cell immunology arts, where it is immaterial whether the ICAM's or anti-CD11a antibodies are used to provide costimulatory signal to T-cells, one of ordinary skill in the

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art at the time of the invention would have found it obvious to substitute anti-CD11a antibodies for the ICAM's of Webb et al.

19. Claims 19, 20, 22, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Butler et al. (*J. Immunol.*, Oct. 2002, Vol. 169: 3700-3709).

Webb et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 11 above). Webb et al. further teaches that activation of T-cells is characterized by proliferation of the responsive T cell population coordinated with the selective production of cytokines (p16, lines 28-32). The cytokines include IL-2, IL-4, IL-5, IL-10, and IFN- $\gamma$  and different cytokine profiles characterized functional phenotypes of type 1 and type 2 T-cells (p16, lines 8-23).

With respect to claim 22, Webb et al. teaches an array, wherein the MHC molecules comprise class II MHC molecules (p18, lines 20-30).

However, Webb et al. fails to teach an array, further comprising anti-factor antibodies specific for secreted factors, immobilized spatially-distinct areas on the substrate.

Butler et al. teaches a method of detecting secreted cytokines by activated T-cells using cytokine capture assay (see entire document, particularly, p3701, left column, *ELISA and ELISPOT*). The cytokine capture assay of Butler et al. utilizes both

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the activating molecules (anti-CD3 and anti-CD28 antibodies) co-immobilized with cytokine capture antibodies (anti-factor antibodies specific for secreted factors, p3701, left column, *ELISA and ELISPOT*).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include anti-factor antibodies specific for secreted factors co-immobilized on the spatially-distinct areas of the substrate with activating molecules as taught by Butler et al. in the array of Webb et al. in order to perform cytokine capture assay for detecting secreted cytokines by the activated T-cells. The advantage of allowing T-cell activation and capturing of the secreted cytokines following the activation on the same substrate provides the motivation to combine teachings of Webb et al. and Butler et al. with a reasonable expectation of success as the use of co-immobilized MHC molecules complexed with antigen-derived peptides and anti-factor antibodies specific for secreted factors would eliminate additional steps of supernatant harvesting and transferring of the supernatant to another substrate for cytokine detection assay necessary to determine cytokine profile of the activated T-cell populations.

20. Claims 19, 20, 22, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Lehmann et al. (U.S. Patent No. 5,939,281, Aug. 17, 1999).

Webb et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 11

above). Webb et al. further teaches that activation of T-cells is characterized by proliferation of the responsive T cell population coordinated with the selective production of cytokines (p16, lines 28-32). The cytokines include IL-2, IL-4, IL-5, IL-10, and IFN- $\gamma$  and different cytokine profiles characterized functional phenotypes of type 1 and type 2 T-cells (p16, lines 8-23).

With respect to claim 22, Webb et al. teaches an array, wherein the MHC molecules comprise class II MHC molecules (p18, lines 20-30).

However, Webb et al. fails to teach an array, further comprising anti-factor antibodies specific for secreted factors, immobilized spatially-distinct areas on the substrate.

Lehmann et al. teaches a method of detecting secreted cytokines by activated T-cells using cytokine capture assay (see entire document, particularly, column 3, lines 14-36). The cytokine capture assay of Lehmann et al. involves plating both the activating molecules (test antigen peptide) co-incubated with immobilized cytokine capture antibodies (column 3, lines 14-36).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include anti-factor antibodies specific for secreted factors co-immobilized on the spatially-distinct areas of the substrate with activating molecules as taught by Lehmann et al. in the array of Webb et al. in order to perform cytokine capture assay for detecting secreted cytokines by the activated T-cells. The advantage of allowing T-cell activation and capturing of the secreted cytokines following the activation in the same area of the substrate provides the motivation to combine teachings of Webb



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et al. and Lehmann et al. with a reasonable expectation of success as the use of co-immobilized MHC molecules complexed with antigen-derived peptides and anti-factor antibodies specific for secreted factors would eliminate additional steps of supernatant harvesting and transferring of the supernatant to another substrate for cytokine detection assay necessary to determine cytokine profile of the activated T-cell populations.

21. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Butler et al. (*J. Immunol.*, Oct. 2002, Vol. 169: 3700-3709) as applied to claim 19 above, and further in view of Taylor (U.S. Patent No. 6,103,479, Aug. 15, 2000).

Webb et al. in view of Butler et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 19 above). However, Webb et al. in view of Butler et al. fails to teach an array, wherein the array comprises at least about 10, 50, or 100 different MHC-peptide complexes.

Taylor teaches arrays for simultaneous analysis of multiple types of cell interactions as discussed above (see item 16 above).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the substrate of Taylor, which includes each of the spatially-distinct areas surrounded by hydrophobic barrier and having either one type of

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compounds (the same MHC molecules) or a combinatorial of distinct compounds (different MHC molecules) in the array of Webb et al. in view of Butler et al. in order to conduct simultaneous analysis of multiple types of cell interactions. The advantage of using substrate, which allows selective binding of the cells of interest to the spatially-distinct areas only and simultaneous analysis of multiple types of cell interactions provides the motivation to employ the substrate of Taylor in the array of Webb et al. in view of Butler et al. with a reasonable expectation of success as the substrate of Taylor can be used for a variety of cell interactions including lymphocytes such as T-cells.

22. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Lehmann et al. (U.S. Patent No. 5,939,281, Aug. 17, 1999) as applied to claim 19 above, and further in view of Taylor (U.S. Patent No. 6,103,479, Aug. 15, 2000).

Webb et al. in view of Lehmann et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 20 above). However, Webb et al. in view of Lehmann et al. fails to teach an array, wherein the array comprises at least about 10, 50, or 100 different MHC-peptide complexes.

Taylor teaches arrays for simultaneous analysis of multiple types of cell interactions as discussed above (see item 16 above).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ the substrate of Taylor, which includes each of the spatially-distinct areas surrounded by hydrophobic barrier and having either one type of compounds (the same MHC molecules) or a combinatorial of distinct compounds (different MHC molecules) in the array of Webb et al. in view of Lehmann et al. in order to conduct simultaneous analysis of multiple types of cell interactions. The advantage of using substrate, which allows selective binding of the cells of interest to the spatially-distinct areas only and simultaneous analysis of multiple types of cell interactions provides the motivation to employ the substrate of Taylor in the array of Webb et al. in view of Lehmann et al. with a reasonable expectation of success as the substrate of Taylor can be used for a variety of cell interactions including lymphocytes such as T-cells.

23. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Butler et al. (*J. Immunol.*, Oct. 2002, Vol. 169: 3700-3709) as applied to claim 19 above, and further in view of Tom-Moy et al. (U.S. Patent No. 6,235,488, May 22, 2001).

Webb et al. in view of Butler et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 19 above). Webb et al. further teaches that biotinylated MHC molecules can be immobilized on the avidin-coated substrate via biotin-avidin linked interactions with

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the substrate (p81, lines 10-16). However, Webb et al. in view of Butler et al. fails to teach that streptavidin can be used in place of avidin.

Tom-Moy et al. teaches that streptavidin can be a substitute for avidin as discussed above (see item 17 above).

Therefore, Webb et al. in view of Butler et al. meets the limitations of claims 8 and 9 except that it employs avidin rather than streptavidin to coat the substrate surface for immobilization of biotinylated MHC molecules. However, because these two elements were art-recognized equivalents at the time of the invention in the specific binding applications, where it is immaterial whether the avidin or streptavidin is used to bind to a biotin, one of ordinary skill in the art at the time of the invention would have found it obvious to substitute streptavidin for the avidin of Webb et al. in view of Butler et al.

24. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (WO 97/46256, Dec. 11, 1997) in view of Lehmann et al. (U.S. Patent No. 5,939,281, Aug. 17, 1999) as applied to claim 19 above, and further in view of Tom-Moy et al. (U.S. Patent No. 6,235,488, May 22, 2001).

Webb et al. in view of Lehmann et al. teaches an array comprising a substrate and an array of MHC molecules complexed with antigen-derived peptides and costimulatory antibodies immobilized in spatially distinct areas on the substrate as discussed above (see item 20 above). Webb et al. further teaches that biotinylated MHC molecules can be immobilized on the avidin-coated substrate via biotin-avidin

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linked interactions with the substrate (p81, lines 10-16). However, Webb et al. in view of Lehmann et al. fails to teach that streptavidin can be used in place of avidin.

Tom-Moy et al. teaches that streptavidin can be a substitute for avidin as discussed above (see item 17 above).

Therefore, Webb et al. in view of Lehmann et al. meets the limitations of claims 8 and 9 except that it employs avidin rather than streptavidin to coat the substrate surface for immobilization of biotinylated MHC molecules. However, because these two elements were art-recognized equivalents at the time of the invention in the specific binding applications, where it is immaterial whether the avidin or streptavidin is used to bind to a biotin, one of ordinary skill in the art at the time of the invention would have found it obvious to substitute streptavidin for the avidin of Webb et al. in view of Lehmann et al.

### ***Conclusion***

25. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- Burrow et al. (U.S. Patent No. 6,270,772, Aug. 7, 2001) teaches MHC molecules complexed with antigen-derived peptides attached to a solid support such as the surface of a plastic dish, a microtiter plate, a membrane, or beads (see entire document, particularly, column 16, lines 7-15 and column 19, line 15-column 20, line 31).

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- Bousso et al. (*Immunol. Lett.*, 1997, Vol. 59, pp85-91) teaches a method of immobilizing MHC-peptide complexes to a microtiter plate (see entire documents, particularly, p86).
- Cai et al. (U.S. Patent No. 6,225,042, May 1, 2001) teaches method of immobilizing MHC molecules to various solid supports such as plastic microwell plates via avidin-biotin interaction (see entire document, particularly, columns 37 and 38, Example 6).
- Finkel et al. (U.S. PG Pub. No. US 2004/0219605, Filed on Apr. 8, 2003) an array of MHC molecules covalently linked to peptides (see entire document).
- Groves et al. (U.S. PG Pub. No. US 2002/0160505 A1, Oct. 31, 2002 and Filed on Feb. 13, 2002) teaches an array (see entire document) comprising a substrate (p2, paragraph [0019]) and an array of MHC molecules complexed with antigen-derived peptides immobilized in spatially distinct areas on the substrate (p2, paragraph [0028]).
- Hodge et al. (*Cancer Res.*, 1999, Vol. 59, pp5800-5807) teaches a triad of costimulatory molecules (B7-1, ICAM-1 and LFA-3) synergizes to amplify T-cell activation (see entire document).
- Khilko et al. (*J. Biol. Chem.*, 1993, Vol. 268, pp15425-15434) teaches a method of immobilizing antigenic peptides (antigen-derived peptides) to a surface (substrate) followed by binding MHC molecules to the immobilized

antigenic peptides using biotin-streptavidin linkage (see entire document, particularly p15428, left column, Fig. 1B).

- Miwa et al. (U.S. Patent No. 6,630,315, Published as a PCT/JP93/01480 on Apr. 28, 1994 and Filed on Sept. 11, 1997) teaches immobilization of MHC class II molecules on solid support (see entire document).
- Hubermann et al. (U.S. PG Pub. No. US 2002/0094567 A1, July 18, 2002) teaches an array of cell carrier grids comprising multimeric MHC-antigen complex (see entire document, particularly, p2, paragraph [0020]).
- Rhode et al. (U.S. Patent No. 6,232,445, May 15, 2001) teaches an array (see entire document) comprising a substrate (96-well plate, column 55, lines 45-51) and an array of MHC molecules complexed with antigen-derived peptides immobilized in spatially distinct areas on the substrate (column 55, lines 45-51 and column 25, lines 5-8), wherein the MHC molecules comprise Class I MHC molecules, Class II MHC molecules, or Class I and Class II MHC molecules (column 3, lines 36-45).
- Roberts et al. (U.S. PG Pub. No. US 2002/0018766 A1, Feb. 14, 2002) teaches a synthetic antigen-presenting matrix, which can be used to present antigen to effector cells (see entire document, particularly p16, paragraph [01710]).

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27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506.

The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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